# Dark Tobacco and Lung Cancer in Cuba[1,2]

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ABSTRACT—A retrospective epidemiologic study of 826 cytologically and/or histologically confirmed lung cancer cases (219 females and 607 males), 979 hospital controls, and 539 neighborhood controls was undertaken in Havana, Cuba, to investigate whether the high lung cancer mortality rates in this country could be explained by the cigarette and cigar consumption habits, including the smoking of dark-tobacco cigarettes. Relative risk(s) (RR) of lung cancer among cigarette smokers were 7.3 in women and 14.1 in men and increased consistently with various measures of exposure to smoke. The findings suggested that duration of smoking, daily number of cigarettes consumed, and inhalation practices have independent effects. Most Cubans smoked dark tobacco. RR were higher for dark-tobacco users than for light-tobacco users (RR = 8.6 vs. 4.6 for women and 14.3 vs. 11.3 for men), but the differences were reduced after adjustment for amount smoked. Cigarette smoking was associated with all histologic types of lung cancer, although the risk for adenocarcinoma was lower than that for the other types. Men who smoked exclusively cigars had a fourfold risk of lung cancer. Mixed smokers (i.e., cigar and cigarette smokers) had a greater RR than cigarette-only smokers (15.0 vs. 14.1), which was perhaps related to the unusually deep and frequent inhalation of cigar smoke. The data support the hypothesis that smoking patterns account for the higher lung cancer mortality in Cuba than in other Latin American countries.—JNCI 1983; 70:1033–1039.

A report on the health conditions in the Americas in the early 1970's revealed that Cuba had the highest lung cancer mortality rates for women in the American region; age-adjusted rates per 100,000 were 8.7 in Cuba as compared to 5.8 in the United States, 3.5 in Argentina, and 2.3 in Uruguay. Corresponding rates for men were the fourth highest in the American region: they were 24.3 in Cuba as compared to 26.9 in the United States, 27.8 in Argentina, and 25.7 in Uruguay (*1*). Of possible significance is that a high proportion of cigarettes smoked in Latin America are made of a dark, locally grown tobacco that has a higher concentration of phenols and nicotine and is more alkaline than the light Virginia-grown type of tobacco (*2*). Skin painting experiments on mice suggested that refined tar from Colombian dark tobacco has about twice the carcinogenic potential as refined tar from U. S. tobacco (*3*). A study of mortality patterns in 11 Latin American cities showed that La Plata, Argentina, had the highest lung cancer male-adjusted mortality rate (59.0/100,000); the explanation offered was the known high consumption of dark tobacco among the population of this city (*4*). This paper reports results of a case-control study undertaken to evaluate the role of smoking habits in the causation of lung cancer among Cuban women and men.

## METHODOLOGY

A case-control study of lung cancer was conducted in Havana, Cuba, a city of approximately 2 million inhabitants (one-fifth of the country's population). Cases were drawn from patients admitted to all the city's 12 main general hospitals with a tentative diagnosis of lung cancer; females were ascertained from 1978 to 1980 and males from 1979 to 1980. In each of the participating hospitals, a staff member was assigned to ensure prompt identification and reporting of all suspected lung cancer patients to the Central Study Office located at the Institute of Oncology and Radiobiology. Only those patients who had their final diagnosis confirmed by cytology and/or histology were included in the study. To ensure consistency of criteria, an ad hoc Pathology Review Committee performed all typing according to the World Health Organization's Classification of Lung Cancer.

A hospital control selected from patients with a current admission for a non-smoking-related disease was matched to each case by sex, age (±5 yr), hospital of admission, and admission date (±15 days). When several controls were available, the closest in admission date was chosen. Not accepted as controls were patients with diseases such as cancers of the upper digestive and respiratory tracts, pancreas, kidney, and urinary bladder; chronic bronchial disease; duodenal and gastric ulcers; and cardiovascular diseases known to be related to smoking. The main diagnostic categories among female and male hospital controls, respectively, were in percentages: digestive diseases (15.1 and 12.8), malignant and benign neoplasms (21.9 and 23.7), eye diseases (6.4 and 15.6), respiratory diseases including tuberculosis (14.5 and 9.3), traumatisms (7.3 and 15.6), diabetes and metabolic disorders (9.6 and 2.6), and skin diseases (4.1 and 7.3); in smaller proportions were the categories arthritis,

ABBREVIATION USED: RR=relative risk(s).

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asthma, anemia, renal diseases, and other miscellaneous conditions.

For each case residing in Havana, an additional neighborhood control was selected and was matched with regard to place of residence (on the same block or as close as possible), sex, and age (±5 yr) in an effort to adjust for socioeconomic and general environmental factors. Selection of the neighborhood control was achieved through the cooperation of neighborhood community affairs committees who made available listings of residents along with information on sex and date of birth. Initially, two hospital controls were matched to each non-Havana resident case, but this was reduced to one hospital control after the 2d year of the study.

As potential study subjects were identified, interviews were conducted with the use of a standardized structured questionnaire. Data were collected on demographic characteristics: educational level; lifelong smoking, residential, and occupational histories; alcohol consumption; and exposure to cooking fuels. The population proved extremely cooperative, with all persons contacted agreeing to participate in the study.

Although the neighborhood controls were interviewed at home and the cases and hospital controls were interviewed in the hospital, minimal interviewer bias was anticipated since most hospital interviews were not conducted at bedside but in adjacent private surroundings. While complete interviewer blindness would have been impossible to achieve, the interviewers were made aware that the questionnaire was administered only to gather general health and disease data from both hospitalized and nonhospitalized populations.

Data on a total of 826 confirmed lung cancer cases (219 females and 607 males), 979 hospital controls, and 539 neighborhood controls were analyzed with the use of procedures for matched (*5*) and unmatched (*6, 7*) studies. Hospital and neighborhood controls for both female and male cases were quite similar regarding sociodemographic characteristics, such as years of education, marital status, and age at interview (table 1). Furthermore, the distribution of the smoking-related variables in both control groups and the RR of lung cancer resulting from the comparison of cases with either control group with the use of matched or unmatched procedures were also similar. It was decided thenceforth to present only the unmatched analyses in which cases were compared with both types of controls combined into a single group.

Measures of exposure to cigarette smoking (i.e., duration of smoking, number of cigarettes smoked daily, and frequency and depth of inhalation) were based on lifetime information on all cigarette brands used; 92% of the respondents smoked one or two brands, and 7% smoked a total of three brands. Identification of dark- versus light-tobacco smokers was made from reported brands. Measures of exposure to tar were based on information from only the four most popular cigarette brands currently smoked, which were analyzed by the Oak Ridge National Laboratory, Oak Ridge, Tenn., for yields of tar, nicotine, CO, and $CO_2$. Therefore, a substantially smaller number of subjects were available for the investigation of smoke content since only persons consuming exclusively the four brands tested could be used.

TABLE 1.—*Percentage distribution of demographic variables in cases (C), hospital (H) controls, and neighborhood (N) controls*

| Variables | Females,[a] % | | | Males,[b] % | | |
|---|---|---|---|---|---|---|
| | C | Controls | | C | Controls | |
| | | H | N | | H | N |
| Age at interview, yr | | | | | | |
| <40 | 4.2 | 6.8 | 4.6 | 4.0 | 2.9 | 2.6 |
| 40–59 | 40.6 | 42.4 | 38.6 | 29.2 | 28.6 | 26.4 |
| ≥60 | 55.2 | 53.4 | 56.8 | 66.8 | 69.0 | 71.1 |
| Mean age | 59.9 | 59.7 | 60.9 | 63.3 | 63.6 | 64.5 |
| Education, yr | | | | | | |
| <7 | 83.1 | 81.7 | 83.8 | 80.5 | 76.0 | 76.7 |
| 7–9 | 11.9 | 13.0 | 10.8 | 12.5 | 13.2 | 15.9 |
| ≥10 | 5.0 | 5.3 | 5.4 | 7.0 | 10.7 | 7.4 |
| Mean yr | 4.5 | 5.0 | 5.2 | 5.2 | 5.6 | 5.8 |
| Marital status | | | | | | |
| Single | 4.1 | 7.3 | 6.1 | 9.9 | 12.1 | 8.9 |
| Married | 61.6 | 57.3 | 58.5 | 74.9 | 71.1 | 76.2 |
| Divorced | 15.1 | 13.4 | 11.5 | 7.1 | 7.5 | 5.9 |
| Widowed | 19.2 | 22.1 | 24.3 | 8.1 | 9.2 | 9.0 |

[a] The following are the total No. of females in each group: C=219, H=262, and N=148.

[b] The following are the total No. of males in each group: C=607, H=717, and N=391.

## RESULTS

The ages of the lung cancer patients ranged from 23 to 89 years, with approximately one-half of the females and two-thirds of the males 60 years old or over at the time of diagnosis. Education level was similar in all groups, but slightly lower mean years of schooling were found among the cases. Approximately 60% of the women and 75% of the men were married (table 1).

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### Smoking

In this study 167 of the 219 female cases (76.3%) and 595 of the 607 male cases (98.0%) ever smoked regularly, as compared to 31.0 and 80.3% of female and male controls, respectively. The corresponding proportions for female hospital and neighborhood controls were 30.5 and 31.8%, whereas for males they were 80.5 and 80.1%. A total of 12.2 and 8.1% of female and 38.9 and 39.9% of male hospital and neighborhood controls, respectively, smoked cigarettes for 50 years or more. Among case smokers, 1 female and 43 males smoked cigars only. In the following analyses cigar-only and pipe-only smokers were excluded.

TABLE 2.—*RR of lung cancer in cigarette smokers according to kind of tobacco*

| Cigarette smoking | Females | | | Males | | |
|---|---|---|---|---|---|---|
| | No. of cases | No. of controls | RR | No. of cases | No. of controls | RR |
| Nonsmokers | 52 | 283 | 1.0 | 12 | 218 | 1.0 |
| Cigarette smokers | 166[a] | 123[a] | 7.3 | 552 | 709 | 14.1 |
| Dark tobacco | 133 | 84 | 8.6 | 529 | 674 | 14.3 |
| Light tobacco | 16 | 19 | 4.6 | 10 | 16 | 11.3 |
| Both dark and light tobaccos | 16 | 17 | 5.1 | 13 | 19 | 12.4 |

[a] Includes some unknown tobacco kind smoked.



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The overall RR of lung cancer in cigarette smokers were 13 and 14.1 for females and males, respectively. Most respondents who smoked consumed the local dark-tobacco cigarettes exclusively, as reported by 80 and 96% of female and male cases, respectively, and by 68 and 95% of their corresponding controls. There were increased risks of lung cancer in both sexes associated with smoking both light and dark tobaccos, but the excess was greater for dark tobacco (RR=8.6 for dark tobacco vs. 4.6 for light tobacco among females; RR=14.3 for dark tobacco vs. 11.3 for light tobacco among males) (table 2).

With either kind of tobacco, the longer the duration of smoking or the greater the total number of cigarettes consumed the higher the risk, all trends being highly significant ($P<0.001$) (table 3). When gradients of increasing risk for duration of smoking and for number of cigarettes smoked daily were estimated with the use of a logistic model that included linear and quadratic effects, the differences in trend between dark- and light-tobacco users were not statistically significant.

Analysis of all cigarette smokers regardless of the kind of tobacco they favored indicated that cases of both sexes not only had a much higher proportion of smokers than controls, but also smoked for many more years, consumed more cigarettes daily, and were exposed to higher amounts of tar (table 4). Highly significant ($P<0.001$) linear trends in RR for these three measures of cigarette smoke exposure were noticed in both sexes; increases of 6.2-fold, 2.9-fold, and 4.5-fold for duration of smoking, daily cigarette consumption, and lifetime tar exposure, respectively, were found between the lowest and the highest levels of exposure in females; the corresponding increases in males were 4.3-fold, 4.0-fold, and 1.6-fold.

TABLE 4.—*RR of lung cancer by several measures of cigarette smoke exposure*

| Measures | Females | | | Males | | |
|---|---|---|---|---|---|---|
| | No. of cases | No. of controls | RR[a] | No. of cases | No. of controls | RR[a] |
| No. of years of smoking | | | | | | |
| <20 | 13 | 28 | 2.5 | 11 | 48 | 4.2 |
| 20–29 | 18 | 26 | 3.8 | 38 | 61 | 11.3 |
| 30–39 | 31 | 24 | 7.0 | 85 | 165 | 9.4 |
| 40–49 | 47 | 24 | 10.7 | 168 | 182 | 16.8 |
| ≥50 | 57 | 20 | 15.5 | 250 | 253 | 18.0 |
| Mean No. of cigarettes/day | | | | | | |
| 1–9 | 33 | 38 | 4.7 | 16 | 54 | 5.4 |
| 10–19 | 72 | 49 | 8.0 | 217 | 318 | 12.4 |
| 20–29 | 28 | 22 | 6.9 | 126 | 175 | 13.1 |
| ≥30 | 32 | 13 | 13.4 | 193 | 161 | 21.8 |
| Lifetime tar exposure[b] | | | | | | |
| I | 17 | 28 | 3.3 | 56 | 79 | 12.9 |
| II | 33 | 12 | 15.0 | 59 | 65 | 16.5 |
| III | | | | 62 | 56 | 20.1 |

[a] All RR relative to those of nonsmokers; all tests of linear trend, $P<0.001$.

[b] Levels of tar in milligrams for females were: I=<11,000 and II=≥11,000. For males they were: I=<15,640, II=15,640–24,079, and III=≥24,080.

TABLE 3.—*RR of lung cancer in nonsmokers and in dark-, light-, and mixed-tobacco[a] cigarette smokers by duration of smoking and number of cigarettes smoked daily[b]*

| Variable | Females | | | Males | | |
|---|---|---|---|---|---|---|
| | No. of cases | No. of controls | RR | No. of cases | No. of controls | RR |
| Nonsmokers | 52 | 283 | 1.0 | 12 | 218 | 1.0 |
| Duration of dark-tobacco smoking, yr[c] | | | | | | |
| 1–19 | 6 | 15 | 2.2 | 9 | 43 | 3.8 |
| 20–39 | 33 | 31 | 5.8 | 107 | 206 | 9.4 |
| ≥40 | 94 | 38 | 13.5 | 413 | 425 | 17.7 |
| Duration of light-tobacco smoking, yr[d] | | | | | | |
| 1–19 | 5 | 10 | 2.7 | 1 | 4 | 4.5 |
| ≥20 | 11 | 9 | 6.7 | 9 | 12 | 13.6 |
| Duration of mixed-tobacco smoking, yr | | | | | | |
| 1–39 | 12 | 15 | 4.4 | 10 | 12 | 15.1 |
| ≥40 | 4 | 3 | 7.3 | 3 | 7 | 7.8 |
| No. daily, dark-tobacco[c] | | | | | | |
| 1–9 | 26 | 23 | 6.2 | 16 | 50 | 5.8 |
| 10–19 | 64 | 35 | 10.0 | 210 | 304 | 12.6 |
| 20–29 | 19 | 15 | 6.9 | 116 | 165 | 12.8 |
| ≥30 | 24 | 11 | 11.9 | 187 | 155 | 21.9 |
| No. daily, light tobacco[d] | | | | | | |
| 1–19 | 9 | 15 | 3.3 | 2 | 8 | 4.5 |
| ≥20 | 7 | 4 | 9.5 | 8 | 8 | 18.2 |
| No. daily, mixed tobacco | | | | | | |
| 1–19 | 6 | 13 | 2.5 | 5 | 10 | 9.1 |
| ≥20 | 10 | 5 | 10.9 | 8 | 9 | 16.2 |

[a] Mixed tobacco=both dark and light tobaccos.

[b] All tests for linear trend relative to those for nonsmokers. $P<0.001$.

[c] Dark-tobacco smokers exclusively.

[d] Light-tobacco smokers exclusively.

When RR for duration of smoking, daily cigarette consumption, and lifelong tar exposure were each computed with separate adjustment for the other two, there remained a consistent pattern of increasing risk with duration of smoking and mean number of daily cigarettes (table 5). The increasing risk with duration of smoking was greater for females (over fourfold) than for males (twofold), although the increases with the daily number of cigarettes were greater for males. While RR increased with tar intake, the risk patterns were less convincing than for duration of smoking and amount smoked. These results suggest that duration of smoking and number of cigarettes acted independently, whereas risk with tar intake was less clear, due perhaps to the high correlation of tar with duration of smoking. Because of the small number of brands tested and the high correlation between the smoke components, the effects of tar could not be isolated from other constituents of tobacco smoke, such as nicotine, CO, or $CO_2$.

The earlier in life cases began to smoke, and the more frequently and the more deeply they inhaled, the higher were their risks of developing lung cancer, even after control for duration of cigarette use; linear trends were significant and did not differ much between females and males (table 6). Cases of both sexes who reported cessation of smoking 1–4 years prior to interview had an increased risk of lung cancer that declined after the 5th year of smoking cessation.



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TABLE 5.—*RR of lung cancer by several measures of cigarette exposure controlling for each other*

| Control for: | RR for No. of years smoked | | | | | |
|---|---|---|---|---|---|---|
| | Females | | | Males | | |
| | 1–29 | 30–39 | ≥40 | 1–29 | 30–39 | ≥40 |
| No. of daily cigarettes | 1.0 | 2.0 | 4.4[a] | 1.0 | 1.1 | 2.1[a] |
| Tar | 1.0 | 6.7 | 5.8[b] | 1.0 | 1.5 | 1.7[c] |

| Control for: | RR for No. of daily cigarettes | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Females | | | | Males | | | |
| | 1–9 | 10–19 | 20–29 | ≥30 | 1–9 | 10–19 | 20–29 | ≥30 |
| No. of years | 1.0 | 1.2 | 1.2 | 2.3[c] | 1.0 | 2.1 | 2.3 | 3.6[a] |
| Tar | 1.0 | 1.3 | 0.6 | — | 1.0 | 0.8 | 1.9 | 1.3 |

| Control for: | RR for lifetime tar exposure, mg | | | | |
|---|---|---|---|---|---|
| | Females | | Males | | |
| | <11,000 | ≥11,000 | <15,640 | 15,640–24,079 | ≥24,080 |
| No. of years | 1.0 | 1.6 | 1.0 | 1.1 | 1.2 |
| No. of daily exposures | 1.0 | 4.1[b] | 1.0 | 1.3 | 1.2 |

[a] Test for linear trend, $P<0.001$.
[b] Test for linear trend, $P<0.01$.
[c] Test for linear trend, $P<0.05$.

This initial elevated risk may reflect cases who stopped smoking because of respiratory disorders antecedent to clinical lung cancer.

No significant differences were noted between cases and controls of either sex with respect to cigarette butt length or use of filtered cigarettes; most smokers consumed at least three-fourths of the cigarette, and less than 5% of smokers used filtered cigarettes. Cubans usually purchased cigarettes with filters only when the ones without filters were not available; a common practice among the Cubans was to remove the filter before lighting.

TABLE 6.—*RR of lung cancer by age smoking started, frequency and depth of inhalation of smoke, and years since last smoked, adjusted for duration of cigarette use*

| Cigarette smoking | Females | | | Males | | |
|---|---|---|---|---|---|---|
| | No. of cases | No. of controls | RR | No. of cases | No. of controls | RR |
| Age started, yr | | | | | | |
| ≥25 | 23 | 41 | 1.0[a] | 18 | 70 | 1.0[b] |
| 15–24 | 67 | 47 | 1.7 | 217 | 357 | 2.1 |
| <15 | 76 | 35 | 2.4 | 317 | 282 | 3.4 |
| Frequency of inhalation | | | | | | |
| Rarely or never | 24 | 40 | 1.0[b] | 56 | 150 | 1.0[b] |
| Sometimes | 16 | 17 | 1.4 | 52 | 55 | 2.6 |
| Always | 125 | 65 | 2.9 | 442 | 501 | 2.4 |
| Depth of inhalation | | | | | | |
| Never | 19 | 35 | 1.0[b] | 43 | 110 | 1.0[b] |
| Slightly | 26 | 31 | 1.5 | 77 | 109 | 1.9 |
| Medium | 31 | 14 | 3.5 | 65 | 110 | 1.5 |
| Deeply | 90 | 43 | 3.2 | 362 | 378 | 2.4 |
| Years since last smoked | | | | | | |
| Current smokers | 132 | 96 | 1.0 | 451 | 524 | 1.0[c] |
| 1–4 | 19 | 8 | 2.0 | 38 | 36 | 1.2 |
| ≥5 | 15 | 19 | 0.9 | 63 | 149 | 0.6 |

[a] Test for linear trend adjusted for duration of cigarette use, $P<0.05$.
[b] Test for linear trend adjusted for duration of cigarette use, $P<0.001$.
[c] Test for linear trend adjusted for duration of cigarette use, $P<0.01$.

## Histologic Type of Lung Cancer

The four main histologic types of lung cancer were almost equally represented among females; in males the squamous type was predominant (36%), followed by the poorly differentiated type (27%), and the undifferentiated type (23%), whereas adenocarcinoma was by far the less frequent (14%).

The risk of lung cancer increased significantly with longer duration of cigarette smoking for all histologic types ($P<0.001$); the greatest risks were associated with the squamous type in females and the undifferentiated type in males (table 7). In spite of the distributional differences in duration of cigarette use and in histology, the risks in smokers of 30 years or more relative to those in nonsmokers were not much different between the sexes. The RR for 1–29 years of exposure were larger in males for all but the adenocarcinoma type. Thus females had a steeper gradient of RR with years of cigarette consumption than did males for the squamous, undifferentiated, and poorly differentiated types, whereas for adenocarcinoma the gradients with duration were similar in both sexes.

Although squamous, undifferentiated, and poorly differentiated types of lung cancer did not differ significantly among themselves insofar as duration of smoking, females with all these three types were exposed significantly longer to cigarette smoke than those with adenocarcinomas (table 8). Adenocarcinoma was the most common histologic type among nonsmokers (48 and 42% in females and males, respectively) whereas it was infrequently seen among smok-

TABLE 7.—*RR of lung cancer according to duration of smoking and histologic type of lung cancer*[a]

| Duration of smoking, yr | Histologic type | | | |
|---|---|---|---|---|
| | Squamous[b] | Undifferentiated[c] | Poorly differentiated[d] | Adenocarcinoma[e] |
| **Females** | | | | |
| 1–29 | 4.4 | 3.9 | 3.2 | 2.1 |
| 30–39 | 9.4 | 15.6 | 7.8 | 2.7 |
| 40–49 | 31.4 | 20.6 | 5.4 | 4.7 |
| ≥50 | 51.9 | 28.3 | 13.1 | 4.0 |
| **Males** | | | | |
| 1–29 | 15.0 | 26.0 | 6.4 | [illegible] |
| 30–39 | 15.9 | 26.4 | 7.7 | 3.2 |
| 40–49 | 39.5 | 40.7 | 10.8 | 5.3 |
| ≥50 | 42.2 | 50.0 | 10.2 | 5.7 |

[a] Risks relative to those in nonsmokers; all trends were significant, $P<0.001$.
[b] There were 54 females and 219 males with the squamous type.
[c] There were 58 females and 138 males with the undifferentiated type. Inasmuch as there were no nonsmoking cases among the 138 males, one case was added in calculation of RR.
[d] There were 48 females and 165 males with the poorly differentiated type.
[e] There were 58 females and 82 males with adenocarcinoma.



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TABLE 8.—*Percentage distribution of histologic types of lung cancer by duration of cigarette smoking and sex*[a]

| Histologic type[b] | Duration of smoking, yr | | | | | Total No. of each histologic type |
|---|---|---|---|---|---|---|
| | 0 | 1–29 | 30–39 | 40–49 | ≥50 | |
| **Females** | | | | | | |
| Squamous | 11.1 | 9.3 | 9.3 | 29.6 | 40.7 | 54 |
| Undifferentiated | 14.0 | 14.0 | 19.3 | 24.6 | 28.0 | 57 |
| Poorly differentiated | 27.1 | 16.7 | 18.8 | 12.5 | 25.0 | 48 |
| Adenocarcinoma | 43.1 | 17.2 | 10.3 | 17.2 | 12.1 | 58 |
| **Males** | | | | | | |
| Squamous | 1.0 | 7.3 | 11.7 | 32.2 | 47.8 | 205 |
| Undifferentiated | 0.0 | 10.4 | 16.0 | 27.2 | 46.4 | 125 |
| Poorly differentiated | 3.2 | 10.4 | 18.8 | 29.2 | 38.3 | 154 |
| Adenocarcinoma | 6.5 | 6.5 | 15.6 | 28.6 | 42.9 | 77 |

[a] Excludes 1 female and 3 males with tumors of mixed histology.
[b] Test of independence among types 1–3—females: $\chi^2_6$=13.3, $P$=0.10; males: $\chi^2_6$=12.5, $P$=0.13. Test of independence among types 1–3 and 4—females: $\chi^2_4$=20.1, $P$=0.001; males: $\chi^2_4$=8.6, $P$=0.07.

of 50 years or more (12 and 13% in females and males, respectively).

## Cigar Smoking in Males

A separate analysis was done on the 216 male cases and 9 controls who smoked either cigars only or cigars plus cigarettes (mixed smokers). (The 5 females, 1 case and 4 controls, who smoked cigars were excluded from analysis.) The risks of lung cancer in both groups of smokers were significantly greater than those in nonsmokers; those males who smoked only cigars had an overall risk of 4.4 and those males who were mixed smokers had an overall risk of 15.0. Risks increased significantly with duration of cigar smoking in those who smoked only cigars as well as in those who were mixed smokers, but the increases with the number of cigars smoked daily in either group of smokers were not significant (table 9).

TABLE 9.—*RR of lung cancer in male nonsmokers, in male smokers of cigars only, and in male smokers of both cigars and cigarettes by duration of smoking and daily consumption*

| Variables | No. of cases | No. of controls | RR |
|---|---|---|---|
| **Nonsmokers** | | | |
| | 12 | 218 | 1.0 |
| **Cigar-only smokers** | | | |
| Duration of smoking, yr | | | |
| 1–39 | 8 | 49 | 3.0 |
| 40–49 | 9 | 54 | 3.0 |
| ≥50 | 26 | 76 | 6.2[a] |
| Daily consumption | | | |
| 1–2 | 8 | 35 | 4.2 |
| 3–4 | 13 | 75 | 3.2 |
| ≥5 | [illegible] | [illegible] | [illegible] |
| **Mixed smokers[b]** | | | |
| Duration of smoking, yr | | | |
| 1–39 | 78 | 112 | 12.7 |
| 40–49 | 42 | 47 | 16.2 |
| ≥50 | 53 | 51 | 18.9[a] |
| Daily consumption | | | |
| 1–2 | 71 | 88 | 14.7 |
| 3–4 | 56 | 71 | 14.3 |
| ≥5 | 46 | 51 | 16.4 |

[a] Test for linear trend relative to 1–39 yr, $P$<0.05.
[b] Mixed smokers = smokers of both cigars and cigarettes.

TABLE 10.—*RR of lung cancer in male smokers of cigars only by age smoking started, years since last smoked, and frequency and depth of inhalation adjusted for duration of cigar use*

| Variables | No. of cases | No. of controls | RR |
|---|---|---|---|
| Total | 43 | 179 | 4.4 |
| Age started, yr | | | |
| ≥25 | 7 | 34 | 1.0 |
| 15–24 | 17 | 91 | 0.8 |
| <15 | 19 | 54 | 1.2 |
| Frequency of inhalation | | | |
| Rarely or never | 21 | 126 | 1.0[a] |
| Partially | 8 | 20 | 2.3 |
| Always | 14 | 33 | 2.5 |
| Depth of inhalation | | | |
| Never | 17 | 105 | 1.0[b] |
| Slightly | 9 | 42 | 1.3 |
| Moderately | 5 | 17 | 1.8 |
| Deeply | 12 | 15 | 4.9 |
| Years since last smoked | | | |
| Current smokers | 36 | 141 | 1.0 |
| 1–4 | 2 | 13 | 0.7 |
| ≥5 | 5 | 25 | 1.1 |

[a] Test for linear trend, $P$<0.01.
[b] Test for linear trend, $P$<0.001.

Male cases who smoked cigars exclusively began their habit earlier in life than the controls; however, after control for duration it was found that age at which smoking was started or years since cessation of smoking did not influence the risk of lung cancer, although the power to detect effects independent of duration was small. In contrast, the RR did increase significantly with frequency and depth of smoke inhalation even after adjustment for duration of smoking (table 10).

## DISCUSSION

The similarity in smoking prevalence and smoking characteristics between both groups of controls was likely due to the high prevalence of smoking in Cuba and the acceptance of hospital controls whose current admission was for a non-tobacco-related disease. In fact, in a 1979 population-based survey in Havana, the frequency of smoking was found to be 33.0% in women and 78.0% in men over 30 years of age (Marcias Castro I: Personal communication). These smoking prevalences are considerably higher than those reported in the early 1970's for eight other Latin American cities, where the overall frequencies of smoking were 18.5 and 47.8%, respectively, in the age group of 25–74 years, ranging from 6.1% (Lima, Peru) to 28.1% (Santiago, Chile) for females and from 35.4% (Lima) to 55.4% (La Plata) for males (*2*). Furthermore, not only a greater proportion of Cubans than other Latin Americans smoked, but also those who did smoke consumed almost twice as many daily cigarettes, started smoking earlier in life, smoked for more years, and preferred the dark type of tobacco and nonfilter ciga-

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rettes. These differences in smoking patterns and the high risk of lung cancer related to cigarette smoking found in our study indicate that smoking habits may account for the higher lung cancer rate in Cuba than in other areas of Latin America.

On the basis of calculations of attributable risk, we estimate that a maximum of 66% of female and 91% of male lung cancer cases in Cuba are due to smoking. Analyses of other variables, such as place of birth, residence, alcohol consumption, and environmental exposure measured by lifelong presence and type of nearby factories, occupation, and use of cooking fuels, did not discriminate between cases and controls. A separate analysis by residence (Havana vs. not Havana) failed to show a differential risk between lifetime rural or urban residency.

It has been suggested (*3, 4*) that smoking the dark type of tobacco product is more deleterious than smoking the light variety. We did find a higher level of risk linked to smoking dark-tobacco cigarettes, but the excess was reduced after accounting for duration and number of cigarettes smoked daily. However, the power to detect a difference between the tobacco types was small due to the very low proportion of light-tobacco cigarette smokers. It has been assumed that, because of their alkalinity, dark-tobacco cigarettes could not be inhaled as deeply and as frequently as light-tobacco ones, but we found that the tobacco type had no influence on the inhalation practices. We believe that the differential risks by type of tobacco require further exploration, preferably in communities where the discrepancy between proportions of light- and dark-tobacco users is not as extreme as in Cuba.

The RR of lung cancer associated with smoking were lower in women than in men, partly related to lower cigarette consumption by women. The RR tended to be slightly lower in women for all smoking categories, such as number of years smoked, mean number of daily cigarettes consumed, lifetime tar exposure, and age starting to smoke, in agreement with prior reports (*8–11*). However, the sex differential risk disappears in frequently and deeply inhaling females for whom the risk is even slightly higher than that in males. This same finding was noted for squamous cell cancers, the histologic type with the strongest relation to smoking. Hence it appears that no biologic protection is afforded to smoking women, and the lower RR result from somewhat lower average smoke exposure within each of the broad categories of age smoking started, duration of smoking, and daily cigarette consumption.

Although differences in the histologic classification criteria complicate the comparison with data from other studies, most studies have reported a preponderance of adenocarcinoma (*12–16*), squamous type (*17*), undifferentiated type (*18*), or similar proportions of undifferentiated type and adenocarcinoma (*19, 20*) in females. In our study, no histologic type was predominant among females. Among males, however, there was agreement in that the squamous type of cancer appeared to predominate (*15, 21, 22*). Similar to the results in other reports, the gradient in RR was steepest for squamous cell carcinomas, but increased risks were found for all types of lung cancer including adenocarcinoma.

Because male cigarette smokers had a threefold higher risk of lung cancer than cigar-only smokers (14.1 vs. 4.4), it was expected that mixed smokers (i.e., smokers of cigarettes plus cigars) would experience a risk intermediate between the risks of the first 2 groups. However, we found instead that cases who were mixed smokers had a slightly greater risk than those smoking cigarettes only (15.0 vs. 14.1); to account for this unexpected finding, we examined the inhalation practices among cases and controls. Results indicated that 31.7 and 41.5% of all cases who smoked cigars only were frequent and deep inhalers of *cigar* smoke, whereas among those who were mixed smokers the percentages were higher, 54.0 and 60.2%, respectively (table 11). Even greater differences in inhalation practices were observed between both groups of smokers in the controls. Conversely, the inhalation practices of *cigarette* smoke did not differ significantly between smokers of cigarettes exclusively and mixed smokers, except for inhalation frequency among the controls. It thus appears that the manner in which mixed smokers inhaled their cigarette smoke determined the manner in which they also inhaled their cigar smoke, which in turn may explain the high risk among the mixed smokers.

TABLE 11.—*Percentage distribution of inhalation practices in male users of cigars only or cigarettes only and in male smokers of both cigars and cigarettes*

| Inhalation | Percent inhaling[a] | | | |
|---|---|---|---|---|
| | Cigar smoke | | Cigarette smoke | |
| | Cigar only | Mixed[b] | Cigarette only | Mixed[b] |
| **Cases** | | | | |
| Frequency | | | | |
| Never or rarely | 48.8 | 27.3 | 8.8 | 11.8 |
| Part of the time | 19.5 | 18.6 | 8.0 | 13.7 |
| Always or most of the time | 31.7 | 54.0 | 83.1 | 74.5 |
| | $P$=0.02 | | $P$=NS | |
| Depth | | | | |
| Never | 39.0 | 16.8 | 6.5 | 9.4 |
| Slightly | 19.5 | 23.0 | 13.4 | 15.1 |
| Deep or moderate | 41.5 | 60.2 | 80.1 | 75.5 |
| | $P$=0.009 | | $P$=NS | |
| **Controls** | | | | |
| Frequency | | | | |
| Never or rarely | 69.6 | 41.2 | 18.8 | 26.9 |
| Part of the time | 11.7 | 14.6 | 6.9 | 9.9 |
| Always or most of the time | 18.7 | 44.2 | 74.3 | 63.2 |
| | $P$<0.001 | | $P$=0.01 | |
| Depth | | | | |
| Never | 57.9 | 28.9 | 14.1 | 19.0 |
| Slightly | 23.4 | 23.9 | 14.1 | 18.5 |
| Deep or moderate | 18.7 | 47.2 | 71.7 | 62.6 |
| | $P$<0.001 | | $P$=NS | |

[a] NS=not significant.
[b] Both cigars and cigarettes.

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